Early Intervention with Repurposed Drugs to Treat COVID-19

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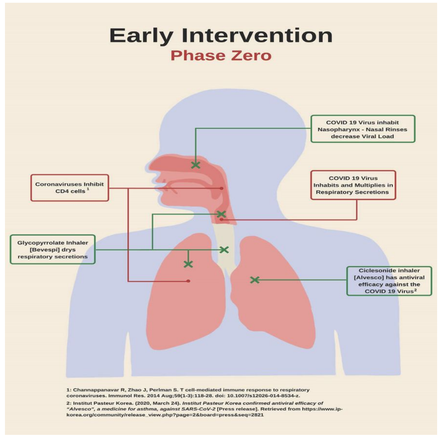
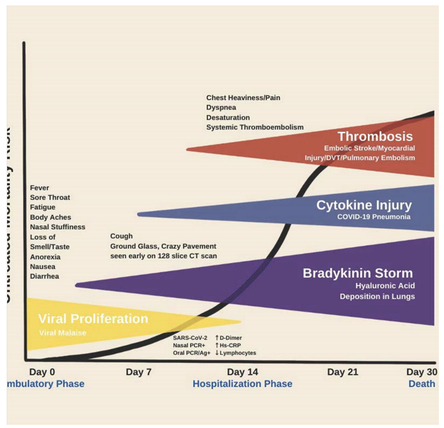
Introduction

1. Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) is a single-stranded RNA virus responsible for the Coronavirus disease 19 (COVID-19) pandemic.
2. A hallmark of the virus is its spike protein, which interacts with the angiotensin-converting enzyme 2 (ACE-2) receptor to invade the cell.
3. After entry, SARS-Cov-2 hijacks existing cellular machinery to self-replicate. The virus binds to the ACE-2 receptors and activates bradykinin production.
4. Repurposed drugs were used to treat COVID-19 early, preventing complications of a deadly cytokine storm that starts around day 10.

Goal: Evaluate the overall effectiveness of these repurposed drugs: individually and in combination



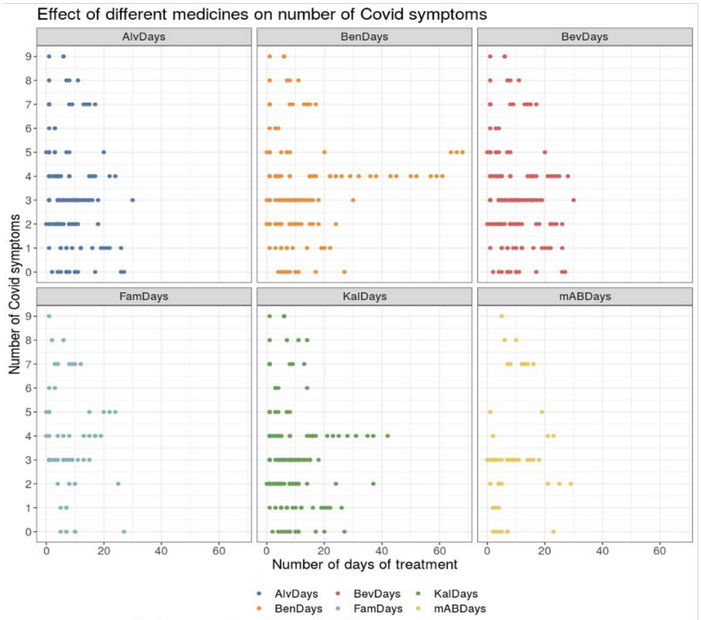
Methods

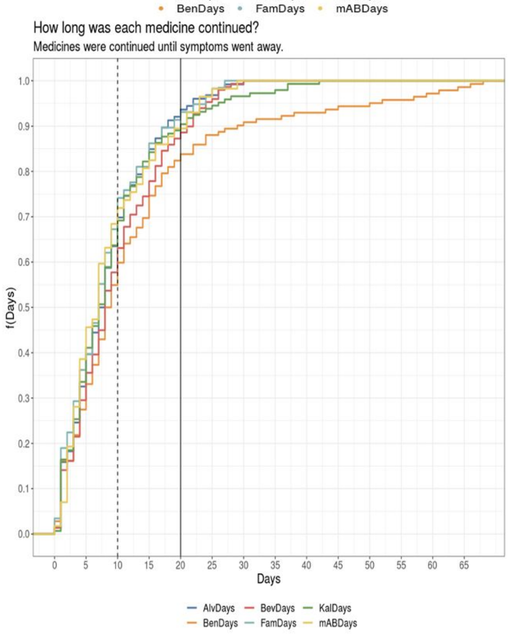


A retrospective observational study to review the efficacy of treatment by measuring symptom resolution. Quantitative symptomatic data was observed for 26 patients (9 patients were 55+) with a lab-confirmed, positive SARS-CoV-2 test. Patients' symptoms improved rapidly in the first ten days. Symptom plot analysis over time with correlation coefficient for each medicine was examined.

Results

- Out of 26 patients, eight (30.8%) were treated with lopinavir/ritonavir, bamlanvimab, glycopyrrolate-formoterol, ciclesonide, and diphenhydramine. Patients experienced a rapid improvement in COVID-19 symptoms within 3-5 days. The correlation coefficients for each medicine and the number of symptoms was determined. The more negative, the faster the resolution of symptoms:
  - Correlation coefficient for Kaletra -0.1407, Bevespi -0.227, Alvesco -0.2191, famotidine -0.1554





Discussion

ACE 2 Enzymes

- ACE 2 Enzymes are significant in this process as they activate bradykinin pathways.
  - COVID enters the cell via the ACE 2 Receptors
  - Pharmacology:
    - The ACE 2 Receptors are blockers
    - Ibuprofen upregulates the ACE 2 Receptors
- Activation of ACE enzymes cause Bradykinin release.
  - Bradykinins increase cell permeability
  - COVID BAL (broncho-alveolar) samples show upregulation of hyaluronan synthases & downregulation of hyaluronidase.
  - Combined with increased lung hyperpermeability results in the formation of hyaluronic acid hydrogel inhibiting gas exchange (crazy pavement ground glass appearance on CT scan).

JAK 2 Receptors

- JAK STAT pathway is the path cytokines released from Intracellular to extracellular.
- JAK 2 receptor blockers prevent the release of cytokines.

Bevespi & Alvesco

- Bevespi is a micelle formulation of glycorrpyrolate a long known respiratory drying agent. It dries up the secretions that Covid lives in.
- Alvesco has been shown in Korean studies to be effective in treating Covid
- In our study of symptom improvement in 24 Covid positive patients Bevespi was effective in reducing symptoms.

Conclusion

- Early treatment, with a combination of the repurposed drugs, interrupts the viral life cycle and prevents the progression into a cytokine storm.
- Treatment in the first 10 days for the COVID-19 virus is highly effective
- It is unknown as to how effective the current vaccines are with the current variants

References

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